

Listing of the Claims:

The following is a complete listing of all the claims in the application, with an indication of the status of each:

1. (Original) A safe for injection, low volume formulation of dantrolene or salts or analogues thereof, for administration to mammals, comprising:
 - a medicament which includes dantrolene or one or more salts or analogues thereof; and
 - a liquid carrier, said medicament being dissolved or dispersed in said liquid carrier, said medicament being present in a concentration wherein 3 to 150 milliliters of liquid carrier provides approximately 500 milligrams of medicament.
2. (Withdrawn) The safe for injection, low volume formulation of claim 1 wherein said medicament includes dantrolene in its free acid form.
3. (Original) The safe for injection, low volume formulation of claim 1 wherein said medicament includes dantrolene in its salt form wherein a counterion to a dantrolene anion is selected from the group consisting of potassium, sodium, ammonium, calcium and magnesium.
4. (Withdrawn) The safe for injection, low volume formulation of claim 1 wherein said medicament includes dantrolene in its salt form wherein a counterion to a dantrolene anion is selected from the group consisting of benzyltrimethylammonium, tetramethylammonium, N-methylpyridinium, tetrabutylammonium, 2-(2,3-dihydroxy-1-propylamino)-quinolizinium, Safranine O, quinolizinium, quinolizinium, 2-carbamoyl-1-methylpyridinium, 2,3-dimethyl-1-phenyl-4-trimethyl-ammonium-3-pyrazolin-5-one, dimethylammonium, 1,3-dimethylimidazolium, 2,3-dimethyl-1-phenyl-4-trimethyl-ammonium-3-pyrazolin-5-one, 2-(1-hydroxy-2-methyl)propyltri-methylammonium, and choline.

5. (Original) The safe for injection low volume formulation of claim 1 wherein dantrolene or one or more salts or analogues thereof is the primary modulator of intracellular calcium present in said medicament.
6. (Original) The safe for injection, low volume formulation of claim 1 wherein said medicament is present in a concentration where 5 to 30 milliliters of liquid carrier provides approximately 300 milligrams of medicament.
7. (Original) The safe for injection, low volume formulation of claim 1 wherein said medicament and said liquid carrier are present together in a colloidal dispersion.
8. (Original) The safe for injection, low volume formulation of claim 7 wherein said liquid carrier is selected from the group consisting of water, a water miscible solvent, glycerol, propylene glycol, dimethylacetamide, ethanol, polyethylene glycol, triethyl citrate, triacetin, monothiolglycerol, or mixtures thereof.
9. (Original) The safe for injection, low volume formulation of claim 8 wherein said polyethylene glycol is selected from the group consisting of PEG 300, PEG 400, and PEG 3350.
10. (Original) The safe for injection, low volume formulation of claim 1 wherein said liquid carrier is selected from the group consisting of water, a water miscible solvent, glycerol, propylene glycol, dimethylacetamide, ethanol, polyethylene glycol, triethyl citrate, triacetin, monothiolglycerol, or mixtures thereof.
11. (Original) The safe for injection, low volume formulation of claim 1 further comprising a surfactant.
12. (Original) The safe for injection, low volume formulation of claim 1 further comprising a stabilizer.

13. (Original) The safe for injection, low volume formulation of claim 1 wherein said medicament and said liquid carrier are present together in a solution.

14. (Original) The safe for injection, low volume formulation of claim 1 wherein said medicament includes crystals of dantrolene or salts or analogues thereof.

15. (Withdrawn) The safe for injection, low volume formulation of claim 1 wherein said medicament includes a sodium channel blocker.

16. (Withdrawn) The safe for injection, low volume formulation of claim 1 wherein said medicament includes a calcium channel blocker.

17. (Withdrawn) The safe for injection, low volume formulation of claim 1 wherein said medicament includes an NMDA receptor antagonist.

18. (Original) The safe for injection, low volume formulation of claim 1 prepared for safe administration by a route selected from the group consisting of intravenous, intramuscular, intrathecal, intraperitoneal, intraocular, and by extracorporeal fluids or circuits.

19. (Original) The safe for injection, low volume formulation of claim 1 wherein at least 95% of particles of medicament in said liquid carrier are no more than 0.8 microns in diameter.

20. (Original) The safe for injection, low volume formulation of claim 1 wherein at least 95% of particles of medicament in said liquid carrier are no more than 0.45 microns in diameter.

21. (Original) The safe for injection, low volume formulation of claim 1 wherein no particles of medicament in said liquid carrier are more than 2 microns in diameter.

22. (Original) The safe for injection, low volume formulation of claim 1 comprising no more than 30 milligrams of mannitol per milligram of dantrolene.
23. (Original) A dry powder formulation of dantrolene which, upon addition of a liquid carrier, produces a safe for injection, low volume formulation of dantrolene or salts or analogues thereof, for administration to mammals, comprising:
a medicament which includes dantrolene or salts or analogues thereof which has physical characteristics such that when combined with a liquid carrier forms a solution or suspension with said medicament being present in a concentration wherein 3 to 150 milliliters of liquid carrier provides approximately 500 milligrams of medicament.
24. (Original) The dry powder formulation of claim 23 wherein said physical characteristics include a drug particle size of less than 0.8 microns and a surface chemistry that ensures dispersibility.
25. (Original) The dry powder formulation of claim 23 comprising no more than 30 milligrams of mannitol per milligram of said dantrolene.
26. (Original) The dry powder formulation of claim 23 wherein said medicament includes dantrolene sodium.
27. (Withdrawn) The dry powder formulation of claim 23 wherein said medicament includes a sodium channel blocker.
28. (Withdrawn) The dry powder formulation of claim 23 wherein said medicament includes a calcium channel blocker.
29. (Withdrawn) The dry powder formulation of claim 23 wherein said medicament includes an NMDA antagonist.
- 30-74. (Canceled)

75. (Withdrawn) The safe for injection, low volume formulation of claim 1 wherein said medicament comprises alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor antagonist.

76. (Withdrawn) The safe for injection, low volume formulation of claim 1 wherein said medicament comprises kainite receptor antagonist.

77. (Withdrawn) The safe for injection, low volume formulation of claim 1 wherein said medicament comprises a free radical scavenger.

78. (Withdrawn) The safe for injection, low volume formulation of claim 1 wherein said medicament comprises a protein kinase inhibitor.

79-80. (Canceled)

81. (Withdrawn) The safe for injection, low volume formulation of claim 1 wherein said medicament comprises a sodium channel blocker.

82. (Canceled)

83. (Currently amended) A composition comprising dantrolene or a salt of dantrolene medicament with water soluble surfactant, wherein said medicament is present in a particulate form of a size of 2 microns or smaller, and wherein said composition is safe for injection or is reconstitutable with liquid so as to be safe for injection, and wherein less than 5 milliliters of liquid carrier provides approximately 500 milligrams of medicament.

84. (Previously presented) The composition of claim 83 wherein the size of over 95% of the particles is 0.8 microns or smaller.

85. (Previously presented) The composition of claim 83 wherein said water soluble surfactant has a solubility of 5 mg/ml or greater.

86. (Previously presented) The composition of claim 83 further comprising a second medicament different from said dantrolene or salt of dantrolene medicament.

87. (Previously presented) The composition of claim 83 further comprising a sufficient quantity of liquid so as to permit administration to a patient of a therapeutically sufficient dose of dantrolene using an auto injector.

88. (Previously presented) The composition of claim 83 further comprising a quantity of liquid which permits administration of a therapeutic dose of dantrolene by injection of said composition to a patient.

89. (Previously presented) The composition of claim 88 wherein said quantity ranges from 3-150 milliliters.

90. (Previously presented) The composition of claim 88 wherein said quantity is 10 milliliters or less.

91. (Previously presented) The composition of claim 88 wherein said quantity is 5 milliliters or less.

92. (Canceled)

93. (Previously presented) A safe for injection, low volume formulation of dantrolene or salts or analogues thereof, for administration to mammals, comprising:

- a medicament which includes dantrolene or one or more salts or analogues thereof; and

- a liquid carrier, said medicament being dissolved or dispersed in said liquid carrier, said medicament being present in a concentration wherein less than 5 milliliters of liquid carrier provides approximately 500 milligrams of medicament.

94. (Previously presented) A dry powder formulation of dantrolene which, upon addition of liquid carrier, produces a safe for injection, low volume formulation of dantrolene or salts or analogues thereof, for administration to mammals, comprising:

a medicament which includes dantrolene or salts or analogues thereof which has physical characteristics such that when combined with a liquid carrier forms a solution or suspension with said medicament being present in a concentration wherein less than 5 milliliters of liquid carrier provides approximately 500 milligrams of medicament.

95. (Previously presented) The safe for injection, low volume formulation of claim 11 wherein the surfactant is a water soluble surfactant.

96. (Previously presented) The dry powder formulation of claim 23 further comprising a surfactant.

97. (Previously presented) The dry powder formulation of claim 96 wherein the surfactant is a water soluble surfactant.

98. (Previously presented) The composition of claim 83 wherein said water soluble surfactant renders the particles dispersible upon the addition of water.

99. (Previously presented) A composition consisting essentially of dantrolene or a salt of dantrolene medicament with water soluble surfactant, wherein said medicament is present in a particulate form of a size of 2 microns or smaller.

100. (Previously presented) A dispersion comprising dantrolene or a salt of dantrolene medicament stabilized in water using water soluble surfactant wherein said dantrolene or said salt of dantrolene medicament is present in a particulate form of a size of 2 microns or smaller.

101. (Previously presented) The composition of claim 83 wherein the water soluble surfactant is selected from the group consisting of benzalkonium chloride,

sodium deoxycholate, myristyl-gamma-picolinium chloride, Polaxamer 188 (Pluronic F-68), Pluronic F-127, polyoxyl castor oil and related PEGylated castor oil derivatives, sorbitan monopalmitate, Pluronic 123, polysorbate, and sodium 2-ethylhexanoic acid.

102. (Previously presented) The composition of claim 83 wherein the dantrolene or salt of dantrolene medicament is sodium dantrolene.

103. (Previously presented) A method for preparing a safe for injection, low volume formulation of dantrolene or salts or analogues thereof, comprising the step of combining a medicament which includes dantrolene or one or more salts or analogues thereof with a liquid carrier and dissolving or dispersing said medicament in said liquid carrier, said medicament being present in a concentration wherein 3 to 150 milliliters of liquid carrier provides approximately 500 milligrams of medicament, said combining step being performed according to one or more of the following: (a) by a single person, (b) by hand shaking, (c) in a single vial or syringe, and (d) in one minute or less.

104. (Previously Presented) A method for preparing a safe for injection, low volume formulation of dantrolene or salts or analogues thereof, comprising the step of combining a medicament which includes dantrolene or one or more salts or analogues thereof with 3 to 150 milliliters of a liquid carrier and dissolving or dispersing said medicament in said liquid carrier, said medicament being present in a concentration wherein 3 to 150 milliliters of liquid carrier provides approximately 500 milligrams of medicament.

105. (Previously presented) The method of claim 104 wherein said combining step is performed according to one or more of the following: (a) by a single person, (b) by hand shaking, (c) in a single vial or syringe, and (d) in one minute or less.

106. (New) The safe for injection, low volume formulation of claim 1 comprising a dose of 250 - 300mg dantrolene sodium and which can be safely administered to a human by a single bolus injection in less than one minute.

107. (New) The safe for injection, low volume formulation of claim 106 comprising a dose of 250 mg of dantrolene sodium.

108. (New) The dry powder formulation of claim 23 present in a single vial to be reconstituted in said vial with 10 ml or less sterile water into a suspension which is safe for injection and which has a concentration of sodium dantrolene of 30 to 80 mg/ml.

109. (New) The dry powder formulation of claim 108 which after reconstitution can be safely administered to a human by a single bolus injection in less than one minute.

110. (New) The safe for injection, low volume formulation of claim 1 wherein said medicament is present at 50 mg/ml.

111. (New) The dry powder formulation of claim 23 wherein the medicament on being combined with liquid carrier is present at 50 mg/ml.